

**Amendments to the Specification:**

Material added is indicated by underlining. Material deleted is indicated by strikethrough.

**Please replace paragraph [0005] on page 1 with the following amended paragraph:**

**[0005]** In accordance with one aspect, a method of treatment for treating, preventing, inhibiting or reducing a biological or immunological response to a reactive chemical agent, biological agent or toxin, by tissue of a subject, comprises administering to a subject in need of such treatment an effective amount of a composition comprising a response-inhibiting agent comprising amino acid sequence LKKTET [SEQ ID NO: 1], a conservative variant thereof, or an agent that stimulates production of an LKKTET [SEQ ID NO: 1] peptide, or a conservative variant thereof, in said tissue, so as to inhibit said response.

**Please replace paragraph [0006] spanning page 1 through page 2 with the following amended paragraph:**

**[0006]** Without being found bound to any specific theory, actin-sequestering peptides such as thymosin beta 4 (T $\beta$ 4 or TB4) and other response-inhibiting agents including actin-sequestering peptides or peptide fragments containing amino acid sequence LKKTET [SEQ ID NO: 1] or conservative variants thereof, promote reversal or prevention of a biological or immunological response from exposure to a reactive chemical agent, biological agent or toxin. The invention is applicable to conditions including, but not limited to, the following: biological or immunological responses of surface tissues such as skin or mucous membranes, dermatologic and other disorders due to allergic reactions, reactions to chemicals and toxins, contact dermatitis, and reactions to plants including, but not limited to, poison ivy, poison oak, and poison sumac; bites of insects including, but not limited to, mosquitoes, fire ants, chiggers,

ticks, bees, spiders, fleas and flies; bites of reptiles, especially venomous reptiles, amphibians, and other animals; contact with various animals with venom on their skin such as poisonous frogs; and allergic reactions of pulmonary and gastrointestinal systems. The invention is also applicable to skin sensitizing agents, psoriasis, atopic dermatitis and eczemas and other conditions that may present with scaling patches and plaques or with bullous and vesicular changes. The invention is also applicable to occupational allergic contact dermatitis, such as but not limited to nickel-associated dermatitis.

**Please replace paragraph [0008] on page 2 with the following amended paragraph:**

**[0008]** In accordance with one embodiment, the invention is a method of treatment for treating, preventing, inhibiting or reducing a biological or immunological response to a reactive chemical agent, biological agent or toxin, by tissue of a subject, comprising administering to a subject in need of such treatment an effective amount of a composition comprising a biological or immunological response-inhibiting agent, which may be a polypeptide comprising amino acid sequence LKKTET [SEQ ID NO: 1], or a conservative variant thereof having biological or immunological response-inhibiting activity, preferably Thymosin  $\beta$ 4, and/or T $\beta$ 4 isoforms, analogues or derivatives, including KLKKTET [SEQ ID NO: 2], LKKTETQ [SEQ ID NO: 3], oxidized T $\beta$ 4, T $\beta$ 4 sulfoxide, N-terminal variants of T $\beta$ 4, C-terminal variants of T $\beta$ 4 and antagonists of T $\beta$ 4.

**Please replace paragraph [0009] spanning page 2 through page 3 with the following amended paragraph:**

**[0009]** Compositions which may be used in accordance with the present invention include agents such as Thymosin  $\beta$ 4 (T $\beta$ 4), and/or T $\beta$ 4 isoforms, analogues or derivatives, including oxidized T $\beta$ 4, T $\beta$ 4 sulfoxide, N-terminal variants of T $\beta$ 4, C-terminal variants of T $\beta$ 4 and antagonists of T $\beta$ 4, polypeptides or peptide fragments comprising or

consisting essentially of the amino acid sequence LKKTET [SEQ ID NO: 1] or conservative variants thereof, having biological or immunological response-inhibiting activity. International Application Serial No. PCT/US99/17282, incorporated herein by reference, discloses isoforms of T $\beta$ 4 which may be useful in accordance with the present invention as well as amino acid sequence LKKTET [SEQ ID NO: 1] and conservative variants thereof having biological or immunological response-inhibiting activity, which may be utilized with the present invention. International Application Serial No. PCT/GB99/00833 (WO 99/49883), incorporated herein by reference, discloses oxidized Thymosin  $\beta$ 4 which may be utilized in accordance with the present invention. Although the present invention is described primarily hereinafter with respect to T $\beta$ 4 and T $\beta$ 4 isoforms, it is to be understood that the following description is intended to be equally applicable to amino acid sequence LKKTET [SEQ ID NO: 1], peptides and fragments comprising or consisting essentially of LKKTET [SEQ ID NO: 1], conservative variants thereof having biological or immunological response-inhibiting activity, and/or T $\beta$ 4 isoforms, analogues or derivatives including oxidized T $\beta$ 4, T $\beta$ 4 sulfoxide, N-terminal variants of T $\beta$ 4, C-terminal variants of T $\beta$ 4 and antagonists of T $\beta$ 4.

**Please replace paragraph [0013] on page 4 with the following amended paragraph:**

**[0013]** Many T $\beta$ 4 isoforms have been identified and have about 70%, or about 75%, or about 80% or more homology to the known amino acid sequence of T $\beta$ 4. Such isoforms include, for example, T $\beta$ 4<sup>ala</sup>, T $\beta$ 9, T $\beta$ 10, T $\beta$ 11, T $\beta$ 12, T $\beta$ 13, T $\beta$ 14 and T $\beta$ 15. Similar to T $\beta$ 4, the T $\beta$ 10 and T $\beta$ 15 isoforms have been shown to sequester actin. T $\beta$ 4, T $\beta$ 10 and T $\beta$ 15, as well as these other isoforms share an amino acid sequence, LKKTET [SEQ ID NO: 1], that appears to be involved in mediating actin sequestration or binding. Although not wishing to be bound to any particular theory, the activity of T $\beta$ 4 isoforms may be due, in part, to the ability to polymerize actin. For example, T $\beta$ 4 can modulate actin polymerization in skin (e.g.,  $\beta$ -thymosins appear to depolymerise F-actin by sequestering free G-actin). T $\beta$ 4's ability to modulate actin polymerization may therefore

be due to all, or in part, its ability to bind to or sequester actin via the LKKTET [SEQ ID NO: 1] sequence. Thus, as with T $\beta$ 4, other proteins which bind or sequester actin, or modulate actin polymerization, including T $\beta$ 4 isoforms having the amino acid sequence LKKTET [SEQ ID NO: 1], are likely to be effective alone or in a combination with T $\beta$ 4, as set forth herein.

**Please replace paragraph [0015] spanning page 4 through page 5 with the following amended paragraph:**

**[0015]** In addition, other response-inhibiting agents or proteins having actin sequestering or binding capability, or that can mobilize actin or modulate actin polymerization, as demonstrated in an appropriate sequestering, binding, mobilization or polymerization assay, or identified by the presence of an amino acid sequence that mediates actin binding, such as LKKTET [SEQ ID NO: 1], for example, can similarly be employed in the methods of the invention. Such proteins include gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, Dnase I, vilin, fragmin, severin, capping protein,  $\beta$ -actinin and acumentin, for example. As such methods include those practiced in a subject, the invention further provides pharmaceutical compositions comprising gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, Dnase I, vilin, fragmin, severin, capping protein,  $\beta$ -actinin and acumentin as set forth herein. Thus, the invention includes the use of an EB-inhibiting polypeptide comprising the amino acid sequence LKKTET [SEQ ID NO: 1] and conservative variants thereof.

**Please replace paragraph [0017] on page 5 with the following amended paragraph:**

**[0017]** T $\beta$ 4 has been localized to a number of tissue and cell types and thus, agents which stimulate the production of an LKKTET [SEQ ID NO: 1] peptide, such as T $\beta$ 4 or another response-inhibiting agent as described herein, can be added to or comprise a composition to effect production of a response-inhibiting agent from a tissue and/or a

cell. Such stimulating agents include members of the family of growth factors, such as insulin-like growth factor (IGF-1), platelet derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor beta (TGF- $\beta$ ), basic fibroblast growth factor (bFGF), thymosin  $\alpha$ 1 (T $\alpha$ 1) and vascular endothelial growth factor (VEGF). More preferably, the stimulating agent is transforming growth factor beta (TGF- $\beta$ ) or other member of the TGF- $\beta$  superfamily. Compositions of the invention may reduce the affects of biological or immunological response to a reactive chemical or biological agent by effectuating growth of the connective tissue through extracellular matrix deposition, cellular migration and vascularization.